SN 09/512,962
Docket No. S-91,732
In Response to Office Action dated January 5, 2004

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claims 1-9 (Cancelled)

10. (Currently Amended) A method for improving an electron density map of an experimental crystal structure, comprising the steps of:

(a) forming a model electron density map from known crystallographic information of an exemplary model crystal structure;

(b) forming model histograms of model electron densities in identified protein and solvent regions of the model electron density map;

(c) fitting a model probability distribution function defined by

~~$$p(\rho_T) = \sum_k w_k \exp\left\{\frac{(\rho - c_k)^2}{2\sigma_k^2}\right\}$$~~

$$\underline{p(\rho_T) = \sum_k w_k \exp\left\{-\frac{(\rho - c_k)^2}{2\sigma_k^2}\right\}}$$

to the model histograms, where k is separately indexed over the protein and solvent regions of the model map, ~~$p(\rho_T)$~~ $\underline{p(\rho_T)}$ is a probability of an electron density at a point, ~~w_k~~ $\underline{w_k}$ is a normalization factor, ρ is electron density, ~~c_k~~ $\underline{c_k}$ is a mean value of ρ, and ~~σ_k~~ $\underline{\sigma_k}$ is a variance of ρ, where the fitting determines the coefficients ~~w_k~~ $\underline{w_k}$, ~~c_k~~ $\underline{c_k}$, and ~~σ_k~~ $\underline{\sigma_k}$;

(d) determining a set of experimental structure factors from x-ray diffraction data for the experimental crystal structure and forming an experimental electron density map;

(e) forming separate experimental histograms of experimental electron densities over protein and solvent regions of the model electron density map;

(f) fitting an experimental probability distribution function defined by

~~$$p(\rho_T) = \sum_k w_k \exp\left\{ \frac{(\rho - \beta c_k)^2}{2\left(\beta\sigma_k^2 + \sigma_{map}^2\right)} \right\}$$~~

$$p(\rho_T) = \sum_k w_k \exp\left\{ -\frac{(\rho - \beta c_k)^2}{2\left(\beta\sigma_k^2 + \sigma_{map}^2\right)} \right\}$$

to separate protein and solvent regions of the experimental histograms, where β is an expectation that an experimental value of ρ is less than a true value and ~~σ_{map}~~ σ_{map} is a variance, where the fitting determines the coefficients β and ~~σ_{map}~~ σ_{map};

(g) determine the overall experimental log-likelihood of the electron density in the protein and solvent regions of the experimental map from the experimental probability distribution function

~~$$LL\left(\rho(\mathbf{x},\{\mathbf{F_h}\})\right) = \ln\left[p\left(\rho(\mathbf{x})|PROT\right) p_{PROT}(\mathbf{x}) + p\left(\rho(\mathbf{x})|SOLV\right) p_{SOLV}(\mathbf{x}) \right]$$~~

$$LL\left(\rho(\mathbf{x},\{\mathbf{F_h}\})\right) = \ln\left[p\left(\rho(\mathbf{x})|PROT\right) pPROT(\mathbf{x}) + p\left(\rho(\mathbf{x})|SOLV\right) PSOLV(\mathbf{x}) \right]$$

where ~~$p_{PROT}(\mathbf{x})$~~ $pPROT(\mathbf{x})$ is the probability that $\mathbf{x}$ is in the protein region and $p\left(\rho(\mathbf{x})|PROT\right)$ is the conditional probability for $\rho(\mathbf{x})$ given that $\mathbf{x}$ is in the protein region, and ~~$p_{SOLV}(\mathbf{x})$~~ $PSOLV(\mathbf{x})$ and $p\left(\rho(\mathbf{x})|SOLV\right)$ are the corresponding quantities for the solvent region;

(h) determine how the experimental log-likelihood of the electron density of the protein and solvent regions of the structure factor experimental electron density map would change as each experimental changes to output a revised log-likelihood of any value of each experimental structure factor;

(i) forming from the revised log-likelihood of experimental structure factor values a new set of structure factors; and

(j) forming a revised experimental electron density map from the revised structure factors.

11. (Presently Presented) The method according to Claim 10, wherein step (a) further includes a step of selecting the model crystal structure to be similar in size, data resolution, and atomic displacement factors to the experimental crystal structure.

12. (Presently Presented) The method according to Claim 10, wherein step (b) further includes a step of identifying protein and solvent regions by designating all points within a selected distance of an atom as "protein" and all other points as "solvent."

13. (Presently Presented) The method according to Claim 11, wherein step (b) further includes a step of identifying protein and solvent regions by designating all points within a selected distance of an atom as "protein" and all other points as "solvent."

14. (Presently Presented) The method according to Claim 10, wherein step (h) includes steps of forming a Taylor's series expansion of the log-likelihood of the experimental electron density map and evaluating terms of the Taylor's series expansion using a Fast Fourier Transform.